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NEUROPSYCHOLOGICA PRINCIPIA BREVITA: AN APPLICATION TO TRAUMATIC (ACQUIRED) BRAIN INJURY [1]

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Summary.—The concepts and discoveries of modern neuroscience now challenge many of the presumptions that influence diagnostic decisions within neurology, psychiatry, and clinical neuropsychology. Many of these presumptions are derived from archaic bivariate models such as the mind-body argument, organic-functional dichotomy, and single lesion–single behavior causality. Thirteen basic principles which may be useful for inferring more reliable and accurate relationships between microstructural function and clinical manifestations are developed.

The history of clinical neuropsychology has been primarily a reversed image of clinical neurology. Both of these scientific disciplines have been dominated by (1) a bivariate methodology that emphasizes a single lesion or a single focus of brain dysfunction as the primary cause of a behavioral effect and (2) the implicit insistence that any behavioral deficits must be chronic (static) and qualitatively distinct to be conspicuous during brief clinical impression. Either hyperactivity or hypoactivity of multiple foci of neurons within brain space or repeated but intermittent displays of pathology have been ignored.

Although a bivariate approach facilitates the utility of nominal (0,1) logical arguments that employ "if-then" statements and exclusionary criteria, it presumes homogeneity of cause both within the logical steps of the diagnostic process and within the etiology of the symptoms. Historical limitations of this approach are exemplified by the attribution of any complex of subtle, changing respiratory symptoms to the diagnosis of "vapors" (late nineteenth century) which overincluded syndromes we now label as tuberculosis, emphysema, pneumonia, influenza, and the common cold. If the antibiotic penicillin had been discovered during the 1890s rather than during the 1940s, the coercive mentality of nominal logic might have rejected its efficacy because the drug would not have cured "all vapors."

When contemporary patients exhibit phasic, multivariate, or subtle changes in complex aggregates of behavior (such as phenomenology or personality) subsequent to a traumatic brain injury or after they have been exposed to a setting in which such an insult is likely to have occurred, the de-

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fault explanation of "psychological" is evoked and, when the behavior dominates the person's expression, a psychiatric source is presumed. The implicit argument by the contemporary medical model which still endorses the mind-body distinction through the use of nosology which emphasizes organic vs functional diagnosis is that "psychiatric" is synonymous with an absence of any organic substrate. A more contemporary and valid approach to the interpretation of neuropsychological profiles of patients who have sustained traumatic (acquired) brain injury is required.

Principle 1: Phenomenological profiles and subjective experiences are determined by the relative mosaic of brain activity.

A person's experiences and behaviors are determined at any given time by those portions of the brain that are most metabolically active (Chugani & Phelps, 1986). Both the themes and the content of the experiences as well as the quantitative variations in the domains of these behaviors will reflect the functional correlates of the portions of the brain which are most active. Under normal conditions the metabolic activity will reflect the active influence of sensory and perceptual stimulation or the selective disinhibition by the prefrontal cortices of subservient cortical and subcortical areas.

Measurements of regional and local metabolic activity within brain space support this principle (Andreasen, 1988; Andersen & Lassen, 1990). For example, the right caudal hemisphere is associated with the perception of visuospatial patterns and a continuum of vigilance. More and specific activation of the right parahippocampal gyrus compared to the left homologous region should evoke more extreme levels of vigilance experienced as anxiety or panic within the contexts which normally stimulate this region of the brain (complex visuospatial settings such as airports, train stations, or open spaces). The strong temporal association between these mild asymmetries in local hemispheric activation and a specific class of panic experiences has been reported by Reiman, Raichle, Butler, Herscovitch, and Robins (1984).

Passive activation of the right parahippocampal region, which is normal during rapid eye-movement sleep (dream sleep) once every 90 min. to 120 min., would be expected to generate experiences that reflect its function and may accommodate the marked visuospatial content, profound meaning, emotional versus categorical (logical) structure, diminished syntactic sophistication and themes of anxiety which characterize the most predominant experience: dreams. Passive activation of expressive functions generates comparable effects. Relative hypermetabolism within the left orbitofrontal cortices and functionally adjacent caudate which are essential for the sequential organization of overt motor (verbal behavior and limb movement) as well as covert verbal (thinking) responses are associated with the extreme manifestation of this function (hyperorganization or obsessive-compulsive behaviors) while hy-

pometabolism is more associated with socially inappropriate displays (Oder, Goldenberg, Spatt, Podreka, & Deecke, 1992).

Principle 2: Aberrant neuronal activation, not necrosis, causes anomalous behaviors.

Experiences and behaviors, including those that occur after a brain injury, are caused by the enhanced activation of neurons and *not* by the absence of neurons. There is no behavior without neuronal activity; the conclusion that unusual behaviors are due to the loss of neurons within the lesion is fallacious. Focal necrosis is associated with the release of control within populations of neurons inhibited by those cells that were damaged. Consequently, *exclusive* attribution of the behaviors to the static lesions (such as localized gliosis or the misnomer "scar" tissue) which are revealed by CT or MRI images is not valid. Instead, the correlative behaviors reflect either the disinhibition of neurons which (1) remain viable within the site of damage, (2) occupy a toroidal or penumbral region (Coyle & Puttfarcken, 1993) along the perimeter of the site, or (3) were primary targets for the axonal destinations of the necrotic neurons. The obvious fourth option is that the behaviors reflect the activation of regions which are not discriminable by either CT or MRI images (Reila & Penry, 1990). If gliosis occurred also in a region within which a subset of neurons also remained viable, then epicritic activation could be associated with significant behavioral correlates.

Principle 3: Any stimulus which affects the synaptic substrate within a functional region will be associated with the complimentary changes in overt and covert behaviors.

All behavior, personality, and complex phenomenological experiences such as the sense of self (Persinger, 1993, 1994) emerge from aggregates of units whose temporal increments and spatial resolutions characterize the level of the synapse and the organization of receptors within this increment of space. Disruptions of synaptic activity by alterations in the densities of different subtypes of receptors, modifications of the temporal transformations or phases of the 0,1 patterns of action potentials (which contain the fundamental information that comprises experience), or changes in the metabolic pathways of any of the multiple neurotransmitters or neuropeptide transducers which occur within a functional aggregate of neurons, are the actual substrates that generate and alter behavior.

However, *any* alterations within any level of brain space that interfere with these critical variables such as alterations in blood flow, capillary perfusion, or invasiveness of glial cells, will modify this substrate. Complete loss of neurons, i.e., a parenchymal discontinuity, necrotic focus, or cystic lesion, is simply an *extreme* component of this continuum. Contrary to the assump-

tion from which some neurological (and litigational) conclusions are made, brain damage can occur *without* loss of consciousness (Parker, 1990).

The first prediction from this principle is that a complete disruption of the synaptic substrate due to microscopic alterations will generate behavioral changes *equal* to those produced by the complete loss of the tissue. This concept appears to have been largely ignored even though experimental studies have shown similar behavioral patterns could be generated by different stimuli whose morphological signatures are antithetic. For example (Persinger, 1971), adult rats which had been exposed prenatally or postnatally to either ionizing radiation or to low-frequency magnetic fields displayed remarkably similar patterns of behavioral deficits even though the former stimulus produced extreme malformations within neuronal architecture while the latter stimulus was associated with no discriminable (at least at 400 × light microscopy) morphological alterations.

This form of microstructural or synaptic alteration will not be obvious by gross macroscopic imaging such as x-ray, CT, or MRI. They may be diffusely revealed by SPECT or PET images if they are correlated with either resolvable microspatial changes in blood flow, oxygen uptake, or glucose metabolism. This option results in a modification of Teuber's dictum "absence of evidence is not evidence of absence" to "absence of structural anomalies by CT or MRI in the context of aberrant neuropsychological deficits is not proof of absence of serious dysfunction or injury."

There is a primary and serious consequence of this corollary that challenges the normal clinical decision within most contexts. Once the clinician has exhausted the available labels for causal attribution, the default diagnosis of "psychological origin" or "psychiatric cause" is elicited simply because there were no evident gross neurological indicators by either clinical observation or by detection of structural anomalies. This decision sequence evokes an artificial distinction of "organic" and "functional." The latter diagnosis, which predominates in psychiatry, has become a pejorative term for "nonphysical" and somehow not controlled by brain function. The implicit thought chain is that the person can "control" the aberrant behavior because the behavior is "not organic" or that the chronic behavioral deficits are due to "family issues." Consequently, patients who display this level of brain disruption are often demeaned by implications such as malingering or displaying "conversion reactions" despite the historical evidence that at least 50% to 70% of the patients with the latter diagnosis ultimately show CT-verifiable lesions or develop neurologic conditions during the next few years (Cummings, 1985).

The second corollary challenges permanency. Whereas complete damage to neuronal somas precludes recovery, their presence increases the probability that neuroplasticity can occur within their processes. However, be-

cause microstructure dictates microfunction, diffuse injuries that permanently alter the protein substrate (particularly receptor densities) or dendrite spine formation because there are direct effects upon either the nuclear or ribosomal machinery will evoke permanent alterations in the microstructure. The consequences of these changes will require the same energetic demands as the previous structure and hence would not be discernable necessarily by metabolic indices. The result would be analogous to the fact that a specific electronic circuit which produces a functional radio signal (systematic and meaningful digital patterns) can employ the same amount of energy as one composed of the same but differently organized circuits, which produces only noise (asystematic and meaningless digital patterns).

Principle 4: Positive symptoms are due to the diminution or dormancy of inhibitory processes.

The major operative process of the brain requires maintained inhibition of neurons. Each display of overt responses and covert behaviors (thoughts) is associated with the selective inhibition of tonic inhibition (disinhibition) and hence excitation. Approximately 25 to 40% of transcerebral synapses involve the inhibitory transmitter gamma amino butyric acid (GABA) whose synthesis and maintenance is directly dependent upon glucose metabolism by the GABA shunt (DeLorey & Olsen, 1994). Those subpopulations of neurons which are most vulnerable to the physical characteristics of the specific trauma such as direct contact with humoral enzymes, decrements in oxygen availability, or the vector of mechanical forces, will be preferentially affected. Because GABA neurons and GABA receptors are both prevalent and among the most vulnerable to subtle alterations in the microenvironment (Bekenstein & Lothman, 1993), changes in these processes and their behavioral correlates will be obvious by contrast enhancement. The manifestations could range from impulsivity to significant shifts in the sleep-wake cycle due to the disruptions in the GABA-driven circadian system (Moore & Speh, 1993).

The selective sensitivity of inhibitory processes to the physical forces (Sloviter, 1987) which accompany the mechanical impact, either directly upon that class of neurons or indirectly through the modification of necessary correlates such as the (thin) caliber of parenchymal vasculature, predisposes the hippocampal formation to dysfunction. The essential process through which this gateway to memory is operative depends almost exclusively upon its capacity to generate inhibitory postsynaptic potentials (Michelson & Wong, 1991). Maintenance of the 0,1 neuroelectrical sequence of coded experience for periods which allow transformation into long-term memory and the initial stages of protein synthesis depends upon critical durations of these potentials.

From this perspective, the phenomenon of *Posttraumatic Amnesia (PTA)* reflects the maintained disruption of inhibitory postsynaptic potentials. Because endogenous hippocampal neurons are more spatially proximal than most neurons, a physical parameter (such as a reduced proportion of extracellular space) which increases the risk of paroxysmal discharges because the enhanced impedance matching associated with smaller intercellular distances encourages local shifts in depolarization, subclinical, i.e., not discernable by qualitative examination of traditional 10–20 scalp electrode arrangements, but protracted microseizures (a variant of complex partial status) within the boundaries of the hippocampal-amygdaloid formations would be expected and would encourage hallucinatory experiences (Ardila & Gomez, 1988). The duration of the Posttraumatic Amnesia and its termination would be the direct consequence of the subclinical microseizures and their termination.

This hypothesis would be compatible with observations that the duration of the Posttraumatic Amnesia is more strongly correlated with the patients' return to premorbid potential than with either the interval of the coma or the duration of retrograde amnesia (Corkin, Hurt, Twitchell, Franklin, & Yin, 1987). Two serious clinical implications result. Firstly, the source of the strong inverse association between the duration of Posttraumatic Amnesia and the ultimate adaptability of the person is a consequence of the protracted subclinical electrical seizures which produce neuronal death (the greater the duration of Posttraumatic Amnesia, the more extensive the cell death). Secondly, selective anticonvulsant treatments following closed-head injury would be essential to attenuate this damage. The occurrence of hallucinatory sequences, which are surprisingly common but less frequently reported because they may have mystical or religious characteristics, are suggestive of the type of electrical activity evoked by direct surgical stimulation (Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994). The contemporary solution of employing antipsychotic neuroleptics (such as haloperidol or chlorpromazine), particularly to patients who are agitated and displaying "schizophreniform" hallucinations (Ardila & Gomez, 1988), would be strongly counterindicated given the risk of cholinergic overshoot and rebound or kindled limbic seizures.

Principle 5: There is an inverse relationship between the severity, chronicity, and clinical conspicuousness of cerebral impairment and the numbers and magnitudes of multifocal dysfunctions.

All sciences contain event words that constitute the major phenomena which define the discipline. Some events contribute to or produce more of the variance in the observations than others within the universal set of the discipline. The more heavily weighted events usually produce chronic, con-

spicuous consequences which are easily detected by brief samples of qualitative observations such as clinical impressions and casual observations. However, the greater the numbers of less weighted elements that aggregate to generate a phenomenon, the more likely the consequences (1) exceed the baseline of normal variation but exist below the just noticeable difference (*jnd*) of qualitative clinical impressions and (2) combine intermittently and aperiodically to evoke transient, extreme impairments. Stated alternatively, the consequences of spatial summation and temporal summation cannot be identified clearly by emphasis upon a single gross measure such as verbal fluency or speed of responding that are observed during one or two brief (20 min.) clinical examinations.

The corollary to this principle is that for a deficit or impairment to be discerned by clinical impression, the equivalent discrepancy must be *approximately two standard deviations* below or above the appropriate mean of the quantitative score for the sign or the symptom. This corollary contains profound clinical effect. Whereas extreme populations, as defined by values that exceed two or three standard deviations, may include 2.5% to 0.3% of the population, individuals with multivariate combinations whose single elements only vary between −1 and −2 constitute 16% of the population. Subtraction indicates that 13.5% of the population who sustain a traumatic brain injury may exhibit combinations of symptoms which are not discernable by crude neurological, neuropsychological, or psychological impressions because each symptom or sign is not individually sufficient to be pathognonomic or conspicuous and the temporal summation of the multivariate sources is intermittent. To argue that intermittent temporal summations of multivariate sources of brain dysfunction are *not* permanent impairments of the person's adaptive potential after a brain injury is analogous to arguing that intractable temporal lobe or frontal lobe (partial complex) epilepsy does not affect the person's quality of life.

Principle 6: Behaviors are due to convergent operations from parallel and multiple sources; identical behavioral manifestations do not represent identical etiologies.

All zeros are not equal in origin. For example, the potential difference (voltage) across a cell membrane can be zero for any number of charges as long as the numbers of charges on both sides are identities. Within the spatial framework of the synapse, decrements in the duration of the sequester between the ligand and receptor contribute to psychological depression. Although the specific mechanisms can vary and may include approximately ten different processes, e.g., aberrant reuptake of the transmitter, excessive catabolism, attenuated precursor synthesis, the net effect upon the pharmacokinetics of the sequestering of the ligand to the receptor is the same and

hence the overt behaviors are identical or indistinguishable within the limited numbers of qualitative criteria of the DSM-IV (American Psychiatric Association, 1994).

The fact that a limited number of response categories determines a small, finite number of possible combinations for diagnostic categories means that real and discrete differences generated by the extremely greater numbers of multifocal neural activations will be overincluded within the same label and considered (erroneously) as homogeneous or as identities. This same conceptual error occurred during early "stress" research when 0,1 changes (hypertrophy or atrophy) in only three or four organs were considered indicative of "generalized stress." The apparent capacity for multitudes of different stimuli to evoke the "same" response lay in the limited numbers of discriminable changes which could occur within only three or four measures.

Comparable convergence occurs within the functional modules of the aggregates of nuclei that generate behavior. The brain is organized as parallel systems which contain multifocal components each of which can contribute differentially to a specific domain of behavior. Although a specific component of each system may primarily control most of the variance in the quantitative occurrence of a behavior (an observation which has given single-lesion studies epiphenomenal validity even though single lesions reduce but rarely totally abolish a behavior), combinations of dysfunction in each of the other less-weighted components of the system can generate a deficit of equal magnitude (Persinger, Bureau, & Peredery, 1994).

The numbers of different brain regions within a system which contribute to an aggregate of symptoms (responses) increase as their relative weighting decreases [an approximate metaphor would be a circle that is divided in half; then the remaining half is divided into halves (two quarters); then the remaining quarter is divided into halves (two eighths) until the smallest practical resolution is obtained]. The resulting equation for this multiple regression dictates that, although the structure with the largest partial regression coefficient will contribute most to the behavior if there is minimal change in the other structures, above-average values for combinations of the lesser structures can generate even *greater* variation in the behavior.

Principle 7: The relationship between the magnitude of neuropsychological impairment and the chronicity of the deficits is not linear.

One of the major premises of psychometric testing is that the patient's performance, as defined by its standard deviation, reflects a standardized numerically linear distance from the reference point (average). Thorough neuropsychological assessments utilize generalized tasks as well as specific procedures from which one infers unique variance; for example, the Tactual

Performance Test is presumed to reflect the functional integrity of the superior parietal lobule once other confounding sources of variance such as finger agility or speed are accommodated. As the patients' scores diverge from the normative mean, the magnitude of the negative standard deviation has been presumed to reflect a continuum of mild, moderate, or severe impairment that is tonic (not changing). The invariance of this assumption is not valid and is analogous to concluding that the behavioral improvement during each daily block on a learning task is caused by the same brain regions simply because the increments of measurement, e.g., trials, time to criterion, each day are also equal.

Graduated scores of the deficits during the execution of a particular task which requires the integrity of a particular brain region reflect graduated states of *hypometabolism* (Pawlik & Heiss, 1989). Brain tissue which is permanently damaged as reflected by massive absence of neurons will exhibit chronic or tonic hypometabolism compared to other regions. Direct SPECT measures may not always be discriminating because the neuronal deficits could be masked by the additive metabolism that accompanies the normal invasiveness of glial cells (reactive gliosis). However, mild to moderate deficits on particular tasks are more likely to reflect clonic or time-varying hypometabolism which is more analogous to an *epileptic focus*. Prolonged periods (hours to days) of hypometabolism are associated with brief periods of *hypermetabolism* that appear to be essential to the formation of GABA and the maintenance of viable physiological conditions.

During most of the patient's behavioral time, the focus would be hypometabolic and the neurocognitive correlates of this region would reflect a "deficit." During much briefer periods, hypermetabolism will occur and the person's behavior and experiences would be dominated by the functional correlates of the brain region (Jibiki & Yamaguchi, 1994). This principle generates a major corollary: *as the multifocal and intermittent* (nonchronic) *characteristics of the acquired brain injury increase, the similarity to partial (temporal lobe and limbic) epilepsies increase.* As a result, persistent phenomenological and other subjective experiences become the nonstereotyped analogue of paraepileptic auras and can be employed to estimate the location of the electrical anomalies.

Classic cases of interictal hypometabolism and ictal hypermetabolism have been reported; patients who exhibit mild right-upper quadrantnopsia interictally will show visual hallucinations that occupy this portion of the visual field during ictal displays (Phelps & Mazziotta, 1985). For patients who have experienced acquired brain injury, brief, compelling ictal-like experiences (Bancaud, *et al.*, 1994) should complement the regions of the brain which are normally hypometabolic and indicate mild to moderate deficits. The sense of a presence along the back or to the left of the person is an

extremely common intrusive and ego-alien experience of patients who have sustained brain trauma (as defined by mild to moderate neuropsychological deficits) and has been hypothesized to be associated with the sudden and brief activation of the right temporoparietal cortices (Persinger, 1994). The report of the phenomenon is compatible with the concept that these experiences are the right-hemispheric equivalent of the linguistic processes within the left hemisphere that generate the sense of self.

Principle 8: Indices of dynamic correlates are more indicative of behavioral deficits than inferences of structural anomalies.

Computer-generated images of structural lesions such as CT or MRI generally reflect static lesions. Attribution of behavioral changes to focal discontinuities of the detection of signals is a correlative but not a causal exercise. Because scar tissue, unless it is irritating adjacent neurons, does not always contain neurons, there may be no behavioral consequence. Dynamic, performance-based tasks such as those employed in thorough neuropsychological assessments are more quantitatively associated with the functional integrity of those portions of the brain.

The CT image of a brain that is dead does not necessarily differ from a brain that is alive. There is no compelling evidence of total concordance between a clinical presentation, which is primarily behavioral, and the occurrence of a region of hypodensity or hyperdensity simply because it is the only discernable anomaly. Because behaviors are dynamic phenomena which depend upon living neurons, the results of standardized neuropsychological tests accurately reflect the regional dysfunction. If a CT-verified region of "scar" tissue is not strongly correlated with adjacent neuronal irritation, then its presence is irrelevant to the clinical symptoms although this loss of potential neurons would limit the patient's flexibility and acquisitional capacity for those functions which are most correlated with the region in which the dysfunctional tissue is located.

Principle 9: Diffuse brain injury simulates the normal effects of aging.

The terminal boundary of the continuum of normal aging is associated with both the loss of neurons and with the regression ("dieback") of higher order dendrites and specific loss of receptor subtypes (Arnsten & Goldman-Rakic, 1985; Weiland & Wise, 1990). They are correlated with the reduced potential of the neuron's metabolic machinery primarily due to the genetically (DNA) determined slowing of protein synthesis or to the exacerbation of the marginal thresholds for hypoxia or demands for nutrients by reductions in capillary capacity, oxygen availability, or intermembrane diffusion; the latter is correlated with shrinkage of the cell soma (Terry & Hansen, 1988). The consequence is macroscopically reflected by the normal enlargement of the lateral ventricles and sulci within the geriatric brain. Brain in-

jury, particularly that evoked by diffuse transmission of mechanical forces through brain space, is associated with similarly diffuse and randomly distributed neuronal dropout and axonal disruption. The effect simulates normal aging.

Consequently, patients who have sustained brain injury often report the experiences reported by the normal older person. These include easier fatiguability, greater recovery times subsequent to mild sickness such as influenza, slower thinking, and the subjective experience of the loss of control over the self and the living environment. Because of the reduction in the synaptic potential, subsequent, even mild injuries, hypoxic insults and their neuroexcitatory correlates (Pokras, 1994) or microvasculature incidents will evoke marked deficits in subsequent behaviors which would not have emerged had the first injury not occurred.

A moderate impairment which is still present two years after primarily diffuse brain damage might accelerate the person's neurocognitive status by 10 to 15 years. Whereas a normal person would undergo the same changes gradually and they would be below the perceptual just noticeable difference (*jnd*), this sudden acceleration for the brain-injured patient would be above the *jnd* and hence conspicuous to both the patient and his family. In general, the more severe the impairment and the older the patient at the time of the trauma, the more rapid the acceleration of neurocognitive aging. Consequently, even an objectively *mild* brain impairment (which simulates a 10-year increment) for a normal 70-year-old patient could evoke dramatic changes in capacity and catastrophic personal responses.

Acceleration of the neuronal aging process (Barnes, 1994) also implies earlier onset of any genetically programmed cell death or disease process. Some patients who have sustained closed-head injuries exhibit an early onset of senile dementia (Gedye, Beattie, Tuokko, Horton, & Korsarek, 1989). The extension of this principle is that patients who are prone to cerebrovascular incidents (stroke) would exhibit this risk years to decades earlier because of the trauma-induced acceleration of neuronal aging. The enhanced deposition of extracellular amyloid precursor protein following activation of muscarinic (acetylcholine) receptors (Nitsch, Slack, Wurtman, & Growdon, 1992), a functional correlate of the age-related decrease in subclasses of adrenergic receptors (Arnsten & Goldman-Rakic, 1985), supports the validity of this principle.

Principle 10: The brain adapts but does not recover after cell death due to brain injury.

Traumas such as mechanical impact, vascular insufficiencies, or excitotoxic damage from the inappropriate influence of transmitters upon the cell membrane (excessive infiltration of free calcium or its release from inacti-

vated storage sites) kill neurons; they do not recover. Permanent compromise of the neuron's metabolic machinery results in severe regression ("dieback") of the most recently developed and (usually) most distal dendritic spines. Consequently, a metaphor of recovery which suggests that the "brain heals" or "returns to normal" is fallacious and misleading to the patient and to the family.

Remaining healthy neurons still maintain capacity to represent experience. Consequently, brain-injured patients learn because the remaining neurons are activated; learning de nouveau is not synonymous with recovery but reflects readaptation. The apparent return to the premorbid behavior is primarily illusionary and is due to the patient's repeated exposure to well-established patterns of stimuli within the rehabilitation setting and overlearned sequences within the home environment. The severity of the deficit is most obvious when the person is placed in a completely novel environment. Because most vocational skills and family patterns are overlearned by the time a middle-aged person sustains a head injury, the severity of the deficit is underestimated. Residual representations of experiences combine with the newly acquired representations such that savings is expressed.

The conclusions and inferences by professionals and by family members are inappropriately influenced by the patients' verbal fluency; however, language is an extremely overlearned skill. Because most verbal social interactions between members of a family are intraverbal sequences, highly ritualized and strongly driven by procedural learning, the absolute severity of the deficits is often underestimated and the unwarranted conclusion of recovery is made. Even in the most severe cases of senile dementia, the last domain to be lost is verbal fluency.

This principle produces two challenges. The first is that the apparent improvement of patients within rehabilitation programs may be confounded by the normal propensity for living systems to adapt to their environment. Attribution of recovery to the interventions would be comparable to concluding that the daily increase in swimming capacity in young amphibians was due to learning rather than to genetic progression (Carmichael, 1926). This interpretation would imply that the apparent improvement, particularly when physical or peripheral limitations accompany brain injury, is an artifact of simply simulating the activity which would have occurred in the absence of the injury. Effectively, the rehabilitative interventions minimize the severity of the sudden change in reinforcement schedules and life-style.

The second challenge relies upon the evidence that time is transformed into spatial matrices within the brain. Temporal sequences, the representation of time's direction, are maintained in the brain as spatial patterns of dendritic spines and receptor aggregates. The contemporary assumption is that the macromolecular units that compose these discrete microstructures

are replaced every few 100 kiloseconds. This capacity would require a representational storage of the *successive temporal* acquisition of these patterns within the DNA of the cell. If this process existed, then reaccess of previous templates, before the traumatic insult, could allow replication of early dendritic patterns.

Principle 11: Most cerebral injuries delay learning but do not eliminate learning if the functional modules remain.

Diffuse loss of neurons reduces the speed of neurocognitive processing and limits the flexibility for adaptation. The consequence is a continuum of deficits within a domain rather than an all-or-none occurrence of a capacity. Patients who have sustained moderate brain injury do not lose the ability to remember; instead they may remember much less. The quantitative severity is usually underestimated unless formal and standardized testing is completed. The patient who has sustained moderate brain injury does not lose the ability to learn new strategies; instead they require more time or more trials to learn the task. The amount of additional time or the number of additional trials is determined by the severity of the impairment. In general, mild, moderate, and severe impairment as employed by Jarvis and Barth (1984) is associated with multiplication factors of 2, 3, and 4.

The caveat to this principle is the patient's position along the continuum of focal damage to diffuse (equally distributed) damage. If there is extreme focal damage within regions of the brain that are functional modules which subserve unique aggregates of behavior, then the proficiency of tasks which require this modular organization will asymptote at the conceptual level of the normal age at which these functions emerge. For example, extreme damage to the right prefrontal cortices may interfere more with the execution of the capacities associated with the normal maturation and functioning of this region. Because this region's conspicuous contribution to the behavior emerges after 13 years to 15 years of age, focal damage to this region has been frequently associated with permanent puerile behaviors and changes in personality that constitute these behaviors.

The optimal procedure by which to discern the neuropsychological profiles must include the direct comparisons of standardized scores for domains of intelligence, general memory, educational achievement, and neurocognitive proficiency (the inverse of impairment) and not simply a single test for memory or for intelligence. The magnitudes of a person's standardized scores for these four major domains are usually comparable. If the person's standardized scores for intelligence, general memory, and educational achievement are within the average range and the neurocognitive proficiency is more than two standard deviations below this range, then a recent brain trauma is very probable. If this level of neurocognitive impairment had been present

from early ontogeny, the person would have been intellectually challenged throughout adulthood.

Principle 12: Transneuronal degeneration contributes to the altered mosaic of neuronal patterns and changes in behavior.

Although the asymptote for neuronal dropout within the cerebrum after a single severe injury occurs within about 40 days (Bigler, Kurth, Blatter, & Abildskov, 1992), the consequences of transneuronal degeneration may continue to occur for years. Transneuronal degeneration involves the reduction in viable activity of neuronal aggregates which typically received input from the destroyed neurons or whose metabolism has been reduced. The first net effect is an upregulation of the receptors (Faden, Demediuk, Panter, & Vink, 1989) conspecific to the inputs. If these aggregates of cells do not contain receptors for other transmitters and modulators (stimulus substitution), they too will atrophy. If they contain other classes of receptors, then the functional output of these cells will be dominated by the disrupted balance.

Transneuronal degeneration within (probably a subset of neurons of) specific reticular thalamic nuclei, portions of the ventral tier or thalamic group and the red nucleus of the mesencephalon have been attributed to the diffuse loss of recurrent input from cortical neurons (Povlishock & Coburn, 1989). That this second level of degeneration and the correlative appearance within MRI and CT scans may require years has been recently suggested for other degenerative disorders such as schizophrenia. These classes of behaviors which comprise this overinclusive diagnosis are generated by disruption within portions of the hippocampus, the extended amygdala, and the thalamus as well as their major cortical projections that include (in the general temporal order of the behavioral appearance of their correlates): the temporal lobes, orbitofrontal lobes, parietal lobes, and dorsolateral prefrontal lobes. Any stimulus, which can range from schedule-induced disruption of receptor aggregates to idiopathic vascular insufficiency to alterations in the cell membrane characteristics that define all neurons within the limbic system because of genetically determined immunocharacteristics, will generate these behaviors (Roberts & Bruton, 1990).

Principle 13: Mild brain impairments are associated with more conspicuous changes in the sense of self and personality than are severe vegetative impairments.

Normal ontogenesis is associated with a cascading increase in the numbers of complex neurocognitive processes that emerge overtly as the person's normal personality (behavioral patterns) and covertly as the "sense of self." Severe impairment (such as dementia), particularly those that significantly alter consciousness or result in gross decline of intellectual level compared to

the preinjury baseline also reduces the numbers of processes to below the critical mass that allows these aggregate phenomena to emerge. Consequently, disruptions in the more complex and subtle processes such as the sense of self and the definition of the self are more likely to be associated with mild multifocal petechial anomalies that may reflect microareas of both hypometabolism and hypermetabolism.

The major prediction is that individuals who sustain mild to moderate impairment, as defined by Jarvis and Barth (1984), particularly within the left temporal and reciprocally associated prefrontal lobes, will exhibit the greatest sense of a loss of the pretraumatic self. This will include rebound depression, grief responses, suicidal ideation, and the feeling of "going crazy." [Because contemporary pharmacological treatments for depression and anxiety were standardized within populations of patients who did *not* sustain brain trauma (and the subsequent microstructural alterations in receptor subtypes), these specific drugs and their dosages could worsen the symptoms.]

On the other hand, severe brain injury which results in gross loss of functions will produce little or no recognition of the loss in the sense of self and minimal changes in personality. Because the person's memories *are* his uniqueness and identity, both as semantic information and the capacity to reconstruct the past by prefrontal integration, the recognition of this change will be modulated primarily by the general memory impairment. Alterations in behavior due to the loss of gross inhibitory domains, resulting in impulsivity, rule breaking, aggressive displays, and other manifestations of disrupted ability to adapt to complex inhibitory schedules (social rules), can be confused with alterations in personality.

The major substrate of personality, sense of self and the awareness of one's self, emerges from the level of the synaptic aggregate. The most compelling empirical support for this principle is the extent to which psychotropic drugs such as antidepressants or some tranquilizers can affect these complex cognitive phenomena. The effects and consequences upon the brain from an acute trauma can be conceived metaphorically as a sequence of overshoots and undershoots of neuronal activity whose frequency increases and amplitude decreases as the numbers of different microregions are recruited and the variations of interference patterns escalate. When the person's brain enters the latter range, the sense of self becomes most vulnerable. For (quantitatively determined) mild injuries, this could occur within one to two months after the incident. For moderate injuries, this interval could be entered months to years after the initial impact. If the severity of the injury produces a state or damage that precludes the operation of those portions of the brain essential for self-awareness or self-monitoring, the stage might never be entered and the awareness of the change in the self would not be encountered.

Mild impairment, particularly multifocal disruptions that evoke cerebrally asymmetric and transient increases in subcortical limbic activity, also increases both the subtlety and complexity of the physiological changes. Activation of the left hemisphere by either direct stimulation or by the relatively increased stimulation due to the paucity of activity within the right hemisphere is immunofacilitative. Consequently, cell membranes or novel pharmacological agents, particularly anesthetics and analgesics, could elicit changes in either humoral or cellular immunity that leads to hypersensitivity and complications from the wide spectrum of subclinical, multivariate disorders now labeled as myalgic encephalomyelitis.

Goldstein (1993) suggested that the spectrum of chronic fatigue syndromes, whose prevalence and incidence predated the contemporary epidemic, are the consequences of diffuse disruptions within those limbic structures that are the major modulators of both the humoral and cellular immunological systems. If elevated complex partial epileptic-like changes are the most frequent consequences of traumatic brain injuries in general and closed-head injuries in particular, then both the explanation for "posttraumatic neurosis" which emerges in some patients after the resolution of the postconcussional syndrome (Miller, 1993) and the traditional recrimination of the patient whose displays of "chronic fatigue" for many years following a "mild head injury" must be re-evaluated. The two syndromes may share similar etiologies.

A shift in the ratio of hemispheric activity which results in a net predominance of the right hemisphere compared to the left would encourage immunosuppression (Biziere, Guillaumin, Degenne, Bardos, Renoux, & Renoux, 1985). Although this period would reduce the severity of inflammatory and allergic responses which could occur when novel antigens or challenges are introduced, the dampening of the response would allow foreign proteins to replicate or aberrant mitotic rates to escalate beyond the protective boundary of the immune system. Tumourgenesis, particularly within the region of the injury, would be expected.

Conclusion

The discrepancy between the bivariate logic, nosology, decision rules, implicit verbal chains and diagnostic determinism of clinical practice, and the empirical principles upon which the brain is organized within spatial increments of cubic nanometers, micrometers, millimeters, and centimeters must be reconciled to increase the accuracy of diagnosis, the efficacy of the initial intervention, and the humanitarian treatment of the patient and the family.

The brain is the primary organ of adaptability to the complex stimulus demands that are defined as the person's social, vocational, and physical en-

vironment. In previous decades, vocational adaption subsequent to brain injury had been facilitated by the redundancy of the tasks, the reliance upon overlearned skills, and the general propensity for employees to remain fixed within a vocational setting. However, as the complexity of our social and vocational environment escalates and the demand for adjustment to completely new settings increases, even minor disruptions, now submerged by the redundant vocational organization of the last decades of the twentieth century, will be evident. Greater appreciation for the subtleties of brain organization is required.

REFERENCES

AMERICAN PSYCHIATRIC ASSOCIATION. *Diagnostic and statistical manual of mental disorders (DSM-IV)*. Washington, DC: American Psychiatric Press, 1994.

ANDERSEN, A. R., & LASSEN, N. A. Single photon emission computerized tomography in temporal lobe epilepsy. In M. Dam & L. Gram (Eds.), *Comprehensive epileptology*. New York: Plenum, 1990. Pp. 375-383.

ANDREASEN, N. C. Brain imaging: applications in psychiatry. *Science*, 1988, 239, 1381-1388.

ARDILA, A., & GOMEZ, J. Complex partial status and schizophrenia. *International Journal of Neuroscience*, 1988, 39, 235-244.

ARNSTEN, A. F. T., & GOLDMAN-RAKIC, P. S. Alpha-2 adrenergic mechanisms in prefrontal cortex associated with cognitive decline in aged nonhuman primates. *Science*, 1985, 230, 1273-1276.

BANCAUD, J., BRUNET-BOURGIN, F., CHAUVEL, P., & HALGREN, E. Anatomical origin of déjà vu and vivid 'memories' in human temporal lobe epilepsy. *Brain*, 1994, 117, 71-90.

BARNES, C. A. Normal aging: regionally specific changes in hippocampal synaptic transmission. *Trends in the Neurosciences*, 1994, 17, 13-18.

BEKENSTEIN, J. W., & LOTHMAN, E. W. Dormancy of inhibitory interneurons in a model of temporal lobe epilepsy. *Science*, 1993, 259, 97-99.

BIGLER, E. D., KURTH, S. M., BLATTER, D., & ABILDSKOV, T. J. Degenerative changes in traumatic brain injury: post-injury magnetic resonance identified ventricular expansion compared to pre-injury levels. *Brain Research Bulletin*, 1992, 28, 651-653.

BIZIERE, K., GUILLAUMIN, J. M., DEGENNE, D., BARDOS, P., RENOUX, M., & RENOUX, G. Lateralized neocortical modulation of the T-cell lineage. In R. Guillemin, M. Cohn, & T. Melnechuk (Eds.), *Neural modulation of immunity*. New York: Raven, 1985. Pp. 81-94.

CARMICHAEL, L. The development of behavior in vertebrates experimentally removed from the influence of external stimulation. *Psychological Review*, 1926, 33, 51-58.

CHUGANI, H. T., & PHELPS, M. E. Maturational changes in cerebral function in infants determined by 18FDG positron emission tomography. *Science*, 1986, 237, 840-843.

CORKIN, S. H., HURT, R. W., TWITCHELL, T. E., FRANKLIN, L. C., & YIN, R. K. Consequences of nonpenetrating and penetrating head injury: retrograde amnesia, posttraumatic amnesia and lasting effects on cognition. In H. S. Levin, J. Grafman, & H. M. Eisenberg (Eds.), *Neurobehavioral recovery from head injury*. New York: Oxford Univer. Press, 1987. Pp. 318-340.

COYLE, J. T., & PUTTFARCKEN, P. Oxidative stress, glutamate, and neurodegenerative disorders. *Science*, 1993, 262, 689-695.

CUMMINGS, J. L. *Clinical neuropsychiatry*. Orlando, FL: Grune & Stratton, 1985.

DELOREY, T. M., & OLSEN, R. W. GABA and glycine. In G. J. Siegel, B. W. Agranoff, R. W. Albers, & P. B. Molinoff (Eds.), *Basic neurochemistry: molecular, cellular, and medical aspects*. (5th ed.) New York: Raven, 1994. Pp. 389-400.

FADEN, A. I., DEMEDIUK, P., PANTER, S. S., & VINK, R. The role of excitatory amino acids and NMDA receptors in traumatic brain injury. *Science*, 1989, 244, 798-800.

GEDYE, A., BEATTIE, B. L., TUOKKO, H., HORTON, A., & KORSAREK, E. Severe head injury hastens age of onset of Alzheimer's disease. *Journal of the American Geriatrics Society*, 1989, 37, 970-973.

GOLDSTEIN, J. A. *Chronic fatigue syndromes: the limbic hypothesis*. New York: Haworth, 1993.

JARVIS, P. E., & BARTH, J. T. *Halstead-Reitan Test Battery: an interpretive guide*. Odessa, FL: Psychological Assessments Resources, 1984.

JIBIKI, I., & YAMAGUCHI, N. Epilepsy and SPECT. *Neuroscience and Biobehavioral Reviews*, 1994, 18, 281-290.

MICHELSON, H. B., & WONG, R. K. S. Excitatory synaptic responses mediated by GABAa receptors in the hippocampus. *Science*, 1991, 253, 1420-1423.

MILLER, L. *Psychotherapy of the brain-injured patient*. New York: Norton, 1993.

MOORE, R. Y., & SPEH, J. C. GABA is the principal neurotransmitter of the circadian system. *Neuroscience Letters*, 1993, 150, 112-116.

NITSCH, R. M., SLACK, B. E., WURTMAN, R. J., & GROWDON, J. H. Release of Alzheimer amyloid precursor derivatives stimulated by activation of muscarinic acetylcholine receptors. *Science*, 1992, 258, 304-308.

ODER, W., GOLDENBERG, G., SPATT, J., PODREKA, I., & DEECKE, L. Behavioural and psychosocial sequelae of severe closed head injury and regional cerebral blood flow: a SPECT study. *Journal of Neurology, Neurosurgery and Psychiatry*, 1992, 55, 475-480.

PARKER, R. S. *Traumatic brain injury and neuropsychological impairment*. New York: Springer-Verlag, 1990.

PAWLIK, G., & HEISS, W-D. Positron emission tomography and neuropsychological function. In E. D. Bigler, R. A. Yeo, & E. Turkheimer (Eds.), *Neuropsychological function and brain imaging*. New York: Plenum, 1989. Pp. 65-138.

PERSINGER, M. A. Pre- and neonatal exposure to cobalt 60 and 0.5 Hz electromagnetic fields and delayed conditioned approach behavior. Unpublished Ph.D. dissertation, Univer. of Manitoba, 1971.

PERSINGER, M. A. Personality changes following brain injury as a grief response to the loss of sense of self: phenomenological themes as indices of local lability and neurocognitive structuring as psychotherapy. *Psychological Reports*, 1993, 72, 1059-1068.

PERSINGER, M. A. Sense of a presence and suicidal ideation following traumatic brain injury: indications of right-hemispheric intrusions from neuropsychological profiles. *Psychological Reports*, 1994, 75, 1059-1070.

PERSINGER, M. A., BUREAU, Y. R. J., & PEREDERY, O. Dissociation between conditioned taste aversion and radial maze learning following seizure-induced multifocal brain damage: quantitative tests of serial vs parallel circuit models of memory. *Physiology and Behavior*, 1994, 56, 225-235.

PHELPS, M. E., & MAZZIOTTA, J. C. Positron emission tomography: human brain function and biochemistry. *Science*, 1985, 228, 799-809.

POKRAS, R. S. A possible role of glutamate in the aging process. *Medical Hypotheses*, 1994, 42, 253-256.

POVLISHOCK, J. T., & COBURN, T. H. Morphopathological change associated with mild head injury. In H. S. Levin, H. M. Eisenberg, & A. L. Benton (Eds.), *Mild head injury*. New York: Oxford Univer. Press, 1989. Pp. 37-53.

REILA, A. R., & PENRY, J. K. Magnetic Resonance Imaging. In M. Dam & L. Gram (Eds.), *Comprehensive epileptology*. New York: Plenum, 1990. Pp. 359-374.

REIMAN, E. M., RAICHLE, M. E., BUTLER, F. K., HERSCOVITCH, P., & ROBINS, E. A focal brain anomaly in panic disorder, a severe form of anxiety. *Nature*, 1984, 316, 683-685.

ROBERTS, G. W., & BRUTON, C. J. Notes from the graveyard: neuropathology and schizophrenia. *Neuropathology and Applied Neurobiology*, 1990, 16, 3-16.

SLOVITER, R. S. Decreased hippocampal inhibition and a selective loss of interneurons in experimental epilepsy. *Science*, 1987, 235, 73-76.

TERRY, R. D., & HANSEN, L. A. Some morphometric aspects of Alzheimer disease and of normal aging. In R. D. Terry (Ed.), *Aging and the brain*. New York: Raven, 1988. Pp. 109-114.

WEILAND, N. G., & WISE, P. M. Aging progressively decreases the densities and alters the diurnal rhythms of alpha 1 adrenergic receptors in selected hypothalamic regions. *Endocrinology*, 1990, 126, 2392-2397.

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